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Patterns of Adult Food Allergy (PAFA-Stage 2)

Submission date
09/12/2021

Recruitment status
No longer recruiting

Registration date
14/03/2022

Overall study status
Completed

Last Edited
21/08/2023

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Many people in the UK suffer from food allergies and intolerances, which cause problems for them when choosing what to eat, buying food, and eating outside the home. Although this is well recognised in children, it affects many adults too. Therefore, the aim of this study is to determine the prevalence of IgE-mediated food allergy in adults aged 18-70 years in a UK-based population. IgE-mediated means that IgE allergy antibodies are a cause of the allergic reaction to a food. The researchers also want to describe the different trajectories of food allergy across the life course, describe adult adverse reactions to foods that are not mediated by IgE and identify potential risk factors for the development of food allergies.

Who can participate?
Adults aged 18-70 years who have participated in the PAFA-Stage 1 study (https://www.isrctn.com/ISRCTN72819770) and have consented to be invited to take part in this study (PAFA-Stage 2).

What does the study involve?
Participants will be invited to a study centre to complete a questionnaire and have an assessment of IgE-mediated sensitisation to common food and inhalant allergens. This will be done using a skin prick test and serology (a blood test). The blood test will be used to determine IgE-sensitisation to food and inhalant (breathed in) allergens and provide banked samples for later DNA analysis and further immunological analysis to confirm and investigate the causes of allergy and other adverse reactions to food.

What are the possible benefits and risks of participating?
Participants who report an adverse reaction to food will benefit from a clearer understanding of whether or not they have a food allergy. They may be eligible to take part in the PAFA-Stage 3 study which will involve a more detailed clinical assessment with a medical doctor to confirm whether they have a food allergy or not. Participants who do not have a food allergy but have other types of allergic or associated respiratory disease will also benefit from a clearer understanding of their allergies and associated respiratory diseases such as asthma. The data gathered in this study will contribute to our understanding of the prevalence and trajectory of food allergy which in turn will help with updating current public health policies regarding food allergy including prevention and treatment.
With regards to the risks of participating, during blood collection, slight discomfort is felt and

bruising can occur occasionally. Some people can feel faint whilst blood is being taken. During skin prick testing, in those whose skin reacts to the allergen, a ‘wheal’ (a small red itchy area) will develop, which is measured and recorded as a positive test. This usually goes away within 10-20 minutes and participants will be offered an antihistamine or steroid cream. There is also a small risk associated with the storage of confidential data and unauthorised disclosure of personal data.

Where is the study run from?
The study is run from GP practices and coordinated by the Universities of Manchester and Southampton with Manchester University NHS Foundation Trust (study sponsor) and the Isle of Wight NHS Trust (UK)

When is the study starting and how long is it expected to run for?
August 2018 to December 2022

Who is funding the study?
Food Standards Agency (UK)

Who is the main contact?
Prof. Clare Mills, clare.mills@manchester.ac.uk

Study website
https://sites.manchester.ac.uk/pafa/

Contact information

Type(s)
Principal Investigator

Contact name
Prof Clare Mills

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
295890

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 50806, IRAS 295890

Study information

Scientific Title
Patterns and prevalence of adult food allergy in a UK population (PAFA-Stage 2)

Acronym
PAFA-Stage 2

Study objectives
To determine the prevalence of probable IgE-mediated food allergy in UK adults aged 18-70 years.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/11/2021, Yorkshire & The Humber - South Yorkshire Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 1048091; southyorks.rec@hra.nhs.uk), REC ref: 21/YH/0262

Study design
Observational; Design type: Cross-sectional

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Other

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Adult food allergy

Interventions

PAFA-Stage 2 follows on from PAFA-Stage 1 community survey where people in the general population aged 18-70 years living in Manchester, Southampton or the Isle of Wight were asked if they experienced any adverse reactions to food. In PAFA-Stage 2 the researchers want to find out more about the adverse reactions to foods that PAFA-Stage 1 respondents reported as well as other types of allergies and associated respiratory diseases like asthma. They are using what is called a "case-control" study design which will help them to identify reasons why some people develop food allergies and others do not. This has been used previously to define the prevalence of food allergy in many studies such as the EuroPrevall project and is acknowledged as providing the robust data required by the funder, the Food Standards Agency (FSA), for the development of evidence-based policy for managing food allergies. The methodology has been developed by the study team and their collaborators which includes laboratory scientists, allergists, GPs, dieticians and a gastroenterologist. It has also been scrutinised by experts external to the project team through the Project Steering Committee convened by the FSA which has patient representation from the Anaphylaxis Campaign. The Anaphylaxis Campaign has also provided additional input into the design of patient-facing documents such as the Patient Information Sheet. PAFA-Stage 2 participants will be selected from the PAFA-Stage 1 respondents who agreed to be re-contacted to take part in PAFA-Stage 2, who do not have dementia or are not in palliative care. Cases will be selected from those with self-reported adverse reactions to foods. Of those who reported no adverse reactions to food and agreed to be contacted for Stage 2, up to two control subjects will be selected per case, selected from the same population area and age-matched where possible. It is estimated that 500 -1,000 eligible participants identified from PAFA-Stage 1 community survey will respond to invitations to be further evaluated in Stage 2. Up to 1,000 age-matched control subjects will also be invited to be evaluated using the same questionnaire and procedures, although precise numbers required to maintain power and confidence in the approach will depend on the response rates. It is anticipated that PAFA-Stage 2 will take between 8-10 months to complete with a further 2 months to analyse data and prepare reports to complete the survey within the project lifetime.

1. Invitation to PAFA-Stage 2 and booking of an allergy assessment visit: Cases and controls will receive a letter from their GP inviting them to take part in PAFA-Stage 2, including a participant information sheet (PIS) describing what is involved in Stage 2. Participants will be invited to contact the research team via either a dedicated phone number or email address to book an appointment. If possible, they will also be provided with a booking system link with the option to book online using either REDCap or an NHS-approved system such as AccuRX. A text message or email reminder will be sent out 1-2 and/or 3-4 weeks after the Stage 2 invitation letter. Those that have not booked their visit after 6 weeks will be contacted directly by phone by the study team. Those who do not have phone or internet access but who wish to participate will be invited to complete the section at the bottom of the invitation letter and return it using an enclosed paid reply envelope; they will then receive an appointment through the post. Those who require the documents in Urdu or Hindi will also have the option to request a study pack in either Urdu or Hindi by completing a section at the end of the invitation letter and returning it using an enclosed paid reply envelope. During the booking process, the study team will establish if there is a potential language barrier for the participant. If a language barrier is identified, participants will be invited to ask a close family member or friend to come with them to their appointment to translate the consent, study procedure, and questionnaire. If no one is available, where possible, a language interpretation service available within primary care will be provided. A text message confirmation of any booked appointments will be sent to participants with a mobile phone number (if provided). This message will include an invitation to reschedule an appointment if necessary.

2. Allergy assessment visit: Each visit is estimated to take a maximum of 55 minutes. During the PAFA-Stage 2 visit, a participant's eligibility to take part in the study will be confirmed, informed regarding reimbursement of reasonable travel expenses and their consent to take part in the allergy assessment recorded. Participants will complete an electronic questionnaire directly using a tablet, have skin prick testing (SPT) to assess sensitisation to common food and inhalant allergen, and (not obligatory) provide a blood sample. The blood samples will be used to (1) isolate plasma/serum for measurement of specific IgE to food and inhalant allergens and for storage for future analysis; and (2) storage of blood cells to allow isolation of DNA for future genetic analysis. Study participants will be given feedback about the test results during the study visit and explain the subsequent follow-up including PAFA-Stage 3 as follows: (a) If a food skin prick test(s) is positive, participants will be invited to take part in the next stage of PAFA (PAFA-Stage 3), which will involve a more detailed clinical assessment with a medical doctor; in this case the GP will be informed. PAFA-Stage 3 is the subject of a separate ethical application. (b) If the food skin prick tests are negative, participants will be told that the research team will wait for the results of the blood test (if one is being done). If the blood tests are positive, the study team will invite the participant to take part in the next stage of PAFA (PAFA-Stage 3) and again inform their GP. If the blood tests are negative, the study team will send this information to the participant's GP together with any advice about what to do next. The participants will be sent a copy of this letter. (c) If the food to which a participant has reported reactions is not on the skin prick testing panel, the study team will arrange for a blood test to this food, if it is available. If these tests are positive, the study team will invite the participant to take part in the next stage of PAFA (PAFA-Stage 3), which will involve a more detailed clinical assessment with a medical doctor. The study team will inform their GP about this. If the blood tests are negative, the study team will send this information to the participant's GP together with any advice about what to do next. The participant will be sent a copy of this letter. (d) If the results are not clear, the participant's case will be discussed with the study doctor and clinical advice will be sent to their GP. The participants will be sent a copy of this letter. Since the PAFA-Stage 2 study visits entail completing a questionnaire and undergoing simple clinical procedures that will take place as far as possible in the community, making use of rooms for research available at GPs or other community spaces close to where participants live. All study visits will be undertaken in a COVID-19 secure manner following the policies in place at the relevant study sites (e.g. GP practices, Manchester University NHS Foundation Trust or the Isle of Wight NHS Trust).

3. Data collection and analysis: All questionnaire responses and allergy assessment results will be gathered together on a secure online research platform called REDCap, allowing for data sharing and analysis of pseudonymised data (personal information such as name and address will not be linked to questionnaire responses). Only those within the study team with permission to view and analyse the data will be granted access using a secure login and password. Interim analysis will be performed on an ongoing basis The information from the questionnaire will be used to find out whether the symptoms participants experience when they eat a particular food are consistent with an IgE-mediated food allergy. Then using a skin prick test and a blood test the researchers will discover if they have made IgE (a process called sensitisation) to that food. Using answers to the questionnaire and the tests they will identify individuals who may have a probable IgE-mediated food allergy and those with a possible non-IgE-mediated food allergy. Interim analysis will be undertaken as data are uploaded into eLab allowing candidates with probable food allergy to be identified and invited for clinical evaluation (including double-blind placebo-controlled food challenge if appropriate) through PAFA-Stage 3 (which will be described in a separate protocol and ethical submission). The analysis will use classical descriptive statistics. The final analysis will then be performed after the collection of follow-up data from the final participant has been completed, data have been checked and cleaned and database lock has taken place. This will include the case-control analysis to define the risk factors for the development of adult-onset food allergy and confounders. Although the researchers will try to

reduce bias it is still likely that other (possibly unobserved) characteristics of those who are willing to be recontacted again for the allergy assessment visit are different from those who do not respond. The researchers will try and take account of this using population weights to account for differences in participants and population as a whole. A repository of data and biological samples will be available in each cohort which can be used for future investigation (e. g. biomarker analysis [serological and/or genetic]), to provide an indication of the extent to which these reactions relate to lactose intolerance and coeliac disease.

Intervention Type
Other

Primary outcome measure
Probable IgE-mediated food allergy, which is defined as all of:
1. Self-reported symptoms associated with consumption of a particular food which are typical of an IgE-mediated food allergy (see list below) [administered questionnaire]
2. Symptoms onset within 2 hours of contact with food [administered questionnaire]
3. Evidence of sensitization to the same food in the form of a positive skin prick test (SPT; ≥3 mm wheal) and/or positive serum specific IgE (≥0.35 kU/L) and/or positive serum specific IgE to component associated with clinical allergy (≥0.35 kU/L) to the same food.

Symptoms considered to be typical of IgE-mediated food allergy include any of the following: itching or tingling in the mouth, lips, ears or throat; swelling of the eyes, lips, or mouth; nettle sting like rash or itchy skin, or red rash; diarrhoea (other than food poisoning); vomiting (other than food poisoning); stomach cramps; hoarseness or swelling of throat; a runny, stuffy nose, or sneezing; red, sore, or running eyes; cough, wheeze, chest tightness, or breathlessness; fainting or dizziness.

Timepoint: December 2022

Secondary outcome measures
Probable non-IgE mediated adverse reaction to food, which is defined as all of:
1. Self-reported symptoms associated with consumption of a particular food which are typical of a non-IgE-mediated adverse reaction to food (see below) [administered questionnaire]
2. Symptoms after 2 hours of consumption [administered questionnaire]
3. No evidence of sensitisation to food in the form of a negative skin prick test (SPT; <3 mm wheal) and/or negative serum specific IgE (<0.35 kU/L) to the same food.

Symptoms typical of non-IgE mediated adverse reaction to food include any of the following: difficulty swallowing; regurgitating stomach contents (stomach contents raising back to the oesophagus or mouth); reflux/ heartburn/indigestion; fainting or dizziness; headaches; stomach cramps; diarrhoea (other than food poisoning); vomiting (other than food poisoning); constipation; other digestive problems (e.g. bloating, wind)

Timepoint: December 2022

Overall study start date
01/08/2018

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. All must be respondents to the PAFA-Stage 1 community survey and consent to be invited to take part in PAFA-Stage 2
2. Cases will be identified as participants who responded to the PAFA-Stage 1 and indicated they have a self-reported adverse reaction to food which is consistent with it being a possible food allergy
3. Controls will be identified as participants who responded to the PAFA-Stage 1 and indicated they do not have a self-reported adverse reaction to food
4. Both cases and controls will be capable of giving informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
Planned Sample Size: 1500; UK Sample Size: 1500

Key exclusion criteria
Adults who have dementia, Alzheimer’s disease, or are receiving palliative care

Date of first enrolment
01/12/2021

Date of final enrolment
04/08/2023

Locations

Countries of recruitment
Netherlands

United Kingdom

Study participating centre

Manchester Royal Infirmary
Cobbett House
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
St Mary's Hospital
Parkhurst Road
Newport
United Kingdom
PO30 5TG

Study participating centre
NIHR CRN: Greater Manchester
Manchester
United Kingdom
M13 9WL

Study participating centre
Bowland Medical Practice
52 Bowland Road
Baguley
Manchester
United Kingdom
M23 1JX

Study participating centre
Bodey Medical Centre
28 Ladybarn Lane
Fallowfield
Manchester
United Kingdom
M14 6WP

Study participating centre
Barlow Medical Centre
Barlow Medical Centre
828 Wilmslow Road

Didsbury
Manchester
United Kingdom
M20 2RN

Study participating centre
St Johns Medical Centre
Altrincham Health & Wellbeing Ctr
31-33 Market Street
Altrincham
United Kingdom
WA14 1PF

Study participating centre
Moss Side Health Centre
Monton Street
Manchester
United Kingdom
M14 4GP

Study participating centre
Tower House Surgery
Tower House
Rink Road
Ryde
United Kingdom
PO33 1LP

Study participating centre
St Francis Practice Ltd
Pilgrims Close
Chandlers Ford
Eastleigh
United Kingdom
SO53 4ST

Study participating centre
Old Fire Station Surgery
68a Portsmouth Road
Weston
Southampton

United Kingdom
SO19 9AN

Study participating centre
The University of Manchester School of Biological Sciences
Manchester Institute of Biotechnology
131, Princess Street
Manchester
United Kingdom
M1 7DN

Study participating centre
The University of Southampton
Paediatric Allergy and Respiratory Medicine
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Amsterdam University Medical Centre (AMC)
Department of Experimental Immunology
K0-134 Meibergdreef 9
Amsterdam
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1105 AZ

Sponsor information

Organisation
Manchester University NHS Foundation Trust

Sponsor details
First Floor, Nowgen Building
29 Grafton Street
Manchester
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United Kingdom
M13 9WU
+44 (0)1612764125
research.sponsor@mft.nhs.uk

Sponsor type
Hospital/treatment centre

Website
https://mft.nhs.uk/

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Government

Funder Name
Food Standards Agency; Grant Codes: FS101174

Alternative Name(s)
The Food Standards Agency, FSA

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
A publication describing the protocol is being prepared and once submitted for publication, it will be made available to ISRCTN to upload.

Planned publication in a high-impact peer-reviewed journal. A summary of the final study results will be placed on the project website hosted by the University of Manchester. An anonymised dataset will be made available by the Food Standards Agency to be accessed through the Government website. Participants may also access the results of the study on these publicly available websites.

Intention to publish date
31/08/2023

Individual participant data (IPD) sharing plan

A fully anonymised dataset will be made available by the Food Standards Agency (planned timeline: by 31/12/2022) to be accessed through the Government website. Publication will be pursued as per the open government policy of the Food Standards Agency in conjunction with their Information Governance risk assessment (previous FSA-funded allergy studies have had some data published openly: https://data.food.gov.uk/catalog/datasets? search=allergy#results).

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No